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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,814	01/12/2007	Judy Lieberman	033393-055222	9795

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EXAMINER	
MCGARRY, SEAN	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
09/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,814	LIEBERMAN ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,28-33 and 35-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,28-33 and 35-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/13/06;10/22/07;12/18/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of SEQ ID NO:15 in the reply filed on 9/15/09 is acknowledged.

Applicants election of a "cardiac cell" and "heart" is noted, however, after search and consideration of the prior art, this species requirement is withdrawn and claims 28, 29 and 41 will be examined herein.

Claims 26, 28-33, and 35-43 are pending and under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26, 28-33, and 35-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al [Am J Physiol Heart Circ Physiol Vol. 284:H456-H463, 2003, first published 10/21/2002, cited by applicant]Song et al [Nature Medicine Vol.9(3):347-351, cited by applicant], Schnurr et al [European Surgical Research Vol. 33:327-333, 3/28/2001], Wang et al [Transplantation Proceedings Vol.35:1594-1595, 2003, cited by applicant], and Khvorhova et al [US20070031844].

The invention is as set forth in the claims.

Lee et al have taught that Fas is a critical mediator of cardiac myocyte death during ischemia-reperfusion injury in vivo. It was shown that in mice without active Fas were less susceptible to infarct size than in mice with Fas when fasL was administered to injury heart tissue. It is taught that the ablation of Fas signaling strikingly reduces infarct size during ischemia-reperfusion *in vivo*. It is asserted that the Fas death pathway is critical for myocyte killing and the full development of MI during ischemia-reperfusion in vivo.

Song et al have taught the use of siRNA compounds to inhibit Fas expression and inhibit apoptosis in mice in vivo. It has been taught that siRNA inhibited Fas in hepatocytes. It is taught that siRNA was administered by intravenous injection. Song et al have taught that siRNA inhibition of Fas protects mice from fulminant hepatitis.

Schnurr et al have taught that Fas is upregulated in livers of non-heart-beating donors[NHBD]. Schnurr et al have taught that hepatocytes in livers from NHBD have an

upregulation of Fas an will prime the cells to eventually undergo apoptosis upon reperfusion in vivo. It is asserted that therapeutic modulation of the Fas-pathway, aiming to normalize the hepatocyte susceptibility towards Fas-related signal transduction, must be considered to protect NHBD livers.

Wang et al have shown that siRNA inhibition of Fas reduces apoptotic cell death of allogenic-transplanted hepatocytes in Mouse spleen. It is taught that this may provide fro inhibition of acute rejection after implantation.

Khvorhova et al have disclosed SEQ ID NOS: 32,033; 32,133; 32,232; 32,331; 32,731; 32,631; 32,531; and 32,430 which are all siRNA compounds targeting Fas and each of comprises the instant SEQ ID NO15. Khvorhova et al have taught that the siRNAs of their invention are selected by means which provide for hyperfunctional siRNAs.

The prior art has therefore taught that it was known to inhibit Fas via siRNA compounds. It was known that inhibition of Fas provides for the inhibition of apoptosis and have taught how this can be utilized in the inhibition of ischemia related injury and also for the treatment of cells and tissues for transplantation. The art has also provided siRNA compounds comprising the instantly recited SEQ ID NO:15 which are taught to be hyperfunctional siRNA targeting Fas. The invention would have been obvious since the art has clearly implicated the Fas pathway in the ischemia and apoptosis and have taught that inhibition of Fas signaling in organs for transplantation can provide for inhibition of rejection.

The invention as a whole would therefor have been *prima facie* obvious to one in the art at the time the invention was made.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31, 32, and 35-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "treating" or "inhibiting" , does not reasonably provide enablement for "preventing". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The instant invention is drawn to the prevention of ischemia-reperfusion injury. The instant specification and the prior art has shown how one in the art may inhibit or down regulate the effects of the Fas-pathway to decrease the effects of ischemia reperfusion injury, however the specification does not provide one in the art with sufficient teachings to "prevent" such injury. Applicant is directed to Lee et al (cited above) where it is shown that prevention of Fas signaling does not prevent ischemic injury, but provides for inhibition of such injury. Applicant is directed to page H461 in particular.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean R McGarry
Primary Examiner
Art Unit 1635

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Primary Examiner, Art Unit 1635